REMARKS

For convenience, pages 2-15 of the Office Action are set forth below, with Applicants' comments interlineated. The Examiner, Dr. Patrick S. Riggins, is thanked for the thoroughness and clarity of his Office action.

Application/Control Number: 09/994,701 Art Unit: 1636

[Page 2] DETAILED ACTION

Election/Restrictions

1.Applicant's election with traverse of Group Ii in the reply filed on 10/14/04 is acknowledged. The traversal is on the ground(s) that Groups I-III are closely related and that examiner did not provide sufficient rationale for requiring restriction. This is not found persuasive because the Groups are distinct as delineated in the Office Action mailed 9/16/04. To reiterate, Group I is drawn to a composition and Groups II and III are distinct methods of using that composition. The steps required to carry out the two different methods are not coextensive and a thorough search of the composition of Group I and the varying method steps of Groups II and III would be burdensome. In response to the argument that support was not provided for the restriction requirement, the restriction requirement has been appropriately supported. For this support, applicant is referred to the paragraphs starting on line 14 of page 2, and line 4 of page 3 of the Office Action mailed 9/16/04. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-9 and 18-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/14/04.

The final requirement is noted. The right to file the nonelected claims in a separate application is reserved.

3. Newly submitted claim 26 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 26 is drawn to a method of making a column while the elected invention is drawn to a method for separating compounds.

These methods share no steps and have completely distinct final products. To search the [Page 3] limitations of claim 26 in addition to the limitations defined by the claims of the elected invention would be burdensome. Accordingly, claim 26 is withdrawn from consideration as

being directed to a non-elected invention. See 37 CFR 1. 142(b) and MPEP § 821.03. Newly added claims 21-25 and 27-33 have been entered and are under examination

Claim 26 is understood to be withdrawn.

Drawings

4. The drawings are objected to because they do not clearly depict the differences reported to be observed. Specifically the graph of Figure 3 is unclear at the axes and the gels of Figures 5, 8, 9, 10, and 11 are too dark to show all bands of interest. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Corrected drawings 3, 5, 8. and 9-11 are enclosed herewith, marked "Replacement Sheet" in the headers. The Figures of gels are photographs rather than drawings and are difficult to improve in quality without re-touching. Figures 5, 8, 9, 10 and 11 are now improved by locating an earlier electronic copy. Figures 5 and 8 are the best available, and are they not essential to an understanding of how to practice the invention.

[Page 4]

Specification

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Applicants' Attorney has re-reviewed the specification.

6. The disclosure is objected to because of the following informalities:

a. sequences listed in the specification have not been identified by SEQ ID NO. Examples of this can be found in paragraphs 169, 171, and 173.

The specification has been amended to add SEQ ID NO sequence numbers in each of the above paragraphs.

b. page 44, paragraph 186 and page 45, paragraph 189 improperly label figures 5 and 8, respectively. In both instances, lanes are described through lane 8 despite the fact that only 6 lanes are present on either gel. Additionally, the figure 5 description lacks any mention of lanes 1, 2, and 4, while the figure 8 description lacks any mention of lanes 1, 3, and 4.

The specification has been amended to insert correct captions.

b. the table that appears on pages 10-13 includes reference to references numbers 25,28,32,35, and 37 whereas the listing of references appearing at the end of specification only lists references through number 22.

The references have been cancelled from the Table.

d. page 26, paragraph 118 discusses using IMAC to purify "PNA". There is no definition of PNA and as such it is unclear what this refers to. Appropriate correction is required.

A definition of "PNA" has been inserted into the Specification: "Peptide Nucleic Acid (PNA) from e.g. Eurogentec, a member of the Licensed Providers of PNA.

Claim Objections [Page 5]

7. Claims 17, 21, 23, 24, 27, 30, and 33 are objected to because of the following informalities:

a. claims 21,23,24, and 27 contain improper punctuation. From MPEP 608.01(m):

"Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations."

Claims 21, 24, and 27 do not end in a period, and claim 23 contains an internal period.

b. claim 30, line 6 inappropriately contains the word "thee". Appropriate correction is required.

The word "drugs" has been corrected to read –drug—in Claim 17.

A period has been inserted at the end of Claims 21, 24 and 27. The internal period has been replaced in Claim 23.

The word "thee" has been corrected to read --the-- in Claim 30, line 6.

> *8. Applicant is advised that should claims 10, 12, 13, 15, 16, and 18 be found allowable, claims 21, 27, 28, 31, 32, and 33 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).*

The Examiner is thanked for this caution, and Claims 21, 27, 26 and 31-33 have been amended to avoid possible duplication.

> ***Claim Rejections - 35 USC § 112-2***
> *9. The following is a quotation of the second paragraph of 35 U.S.C. 112:*
> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*
> *10. Claims 17, 28, 29, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. [Page 6]*
> *11. Claims 17 and 33 contain improper alternative language, as the claims state: "selected from the group consisting of" but proceed to identify the group with or terminology. This constitutes improper Markush format. See MPEP 2173.05(h). Additionally, the claims are indefinite because first they identify that the compound is an AIDS drug, yet then list coenzyme A as one of the members of the group. This is indefinite because coenzyme A is not an AIDS drug, so it is unclear if this claim is drawn to the purification of AIDS drugs or not.*

In Claims 17 and 33, "or" has been amended to --and--. Additionally, the words: "Coenzyme A" have been cancelled from those Claims. "Coenzyme A" is a natural molecule in all living things. It has a structure that will stick to metal affinity adsorbents, but it has been objected-to as not being an AIDS drug.

12. Claim 28 recites the limitation "an effluent from the column" in line 2. There is insufficient antecedent basis for this limitation in the claim. It would appear that applicant intended to have this claim depend from claim 27 rather than claim 10. In the interest of compact prosecution, for the rest of this Office Action, and for paragraph 8 above, claim 28

Claim 28 now depends from Claim 27.

13. Claim 29 recites the limitation "the mixture of compounds" in lines 1 and 4. There is insufficient antecedent basis for this limitation in the claim. It would appear that applicant intended to have this claim depend from claim 27 rather than claim 26. In the interest of compact prosecution, for the rest of this Office Action, claim 29 will be read to depend from claim 27.

Claim 29 now depends from Claim 27.

Claim Rejections - 35 USC § 112-1

14. The following is a quotation of the first paragraph of35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 10, 11,21,22,24, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immobilized metal "ions", does not [Page 7] reasonably provide enablement for immobilized metal "atoms". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. These claims are drawn to a method for separating compounds using "immobilized metal atoms and/or ions". No examples are given and no evidence is provided that would suggest that metal atoms would be capable of separating single stranded from double stranded nucleic acids.

In Claims 10 and 21, "atoms and/or" has been deleted for clarity.

17. The disclosure as filed does not contain sufficient description to enable one of skill in the art to separate unshielded purine/pyrimidine moieties from shielded purine/pyrimidine moieties using IMAC ligands without undue experimentation. A number of factors have been considered in making this assertion that undue experimentation is required to practice this invention as delineated by In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the

amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

18.As these claims are drawn to any "metal atom" they are to be read very broadly. In the specification, on page 2, applicant presents prior art and essentially the groundwork that led the inventors to the idea of purifying nucleic acids by metal affinity chromatography. "Immobilized Metal Affinity Chromatography (IMAC) was introduced by Porath et al. as a means of purifying proteins based on the affinity of their surface-exposed amino acids (especially histidines) for chelated metal ions. The interaction of metal ions with nucleic acids is a long-standing and active field of study. While metal ion binding to nucleic acids is well known, and plays an [Page 8] important role in the function of the widely used cancer drug cisplatin, IMAC has found very limited application in the purification of nucleic acids. Fanou-Ayi and Vijayalakshmi and Hubert and Porath demonstrated the binding of mononucleotides to copper IMAC resins, and histidine conjugated PCR primers have been used to facilitate purification of the resulting histidine-tagged oligonucleotide products, but the potential applications ofIMAC in nucleic acid separation and analysis remain largely unexplored." Here applicant is establishing that IMAC works through the coordination of IMAC ligands by histidine side chains of proteins, or the heterocyclic purine or pyrimidine rings of nucleotide bases. As such, it is the positive charge of the metal cations that is the necessary feature of the IMAC ligand. Metal atoms do not have this cationic nature, and absent evidence to the contrary, would be unable to specifically coordinate either purine/pyrimidine rings of nucleic acids or histidine side chains of proteins. Indeed, Petty states on page 10.11.23 how non-ionic metals are to be avoided in metal affinity chromatography.

"Strong reducing agents such as dithiothreitol should also be avoided because the reduce the Ne+ ions to metallic nickel, forming a brown precipitate."

19. The level of one of skill in the art is high, and as such one of skill in the art would draw the same conclusions pertaining to the ability of metal atoms to purify the compounds of interest.

The specification provides no teachings that would suggest that non-ionic metal atoms could perform this purification function, and the working examples provided all deal with the use of metal ions not metal atoms.

In Claims 10 and 21, "atoms and/or" has been deleted for clarity.

20. When determining if an enablement rejection is proper, one first looks to the specification for teachings which would enable the skilled

artisan to practice the invention. The instant specification provides no teachings with regard to the use of metal atoms in any purification [Page 9] scheme. If it is determined that the specification does not contain the necessary teachings, as in the instant case, one then looks to the prior art for examples of this knowledge being present at the time the application was filed. No such examples exist in this case and indeed Petty teaches away from the use of non-ionic metal atoms. Following the prior art determination one then considers the level of experimentation that would be required in order to practice the claimed invention. As success in using metal atoms to bind to non-shielded purine or pyrimidine moieties is highly unlikely, any attempt by the skilled artisan to practice this invention would required undue levels of experimentation in attempt to overcome this seemingly insurmountable obstacle.

In independent Claims 10 and 21, "atoms and/or" has been deleted for clarity.

21. Claims 14, 15, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for contacting a liquid food stuff, such as a broth, with an !MAC ligand containing substrate, does not reasonably provide enablement for contacting of solid food with an IMAC ligand substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
22.These methods are drawn to a method of purifying food stuffs by removing "nucleic acid contaminants". Again, the Wands factors have been considered in making this rejection. These claims are very broad in their scope as they are drawn to any food stuff. Despite an extensive search no prior art was identified that removed nucleic acids from food stuffs for the purpose of purifying the food. The specification makes no mention of any details relating to the purification of food stuffs using IMAC technology. As such there are no working examples in this regard.
The predominant issue with regard to enablement is that it is exceedingly difficult to envision how one would practice this invention as claimed. It is apparent that IMAC ligand-containing
Page 10 beads could be utilized to remove compounds from a liquid food stuff. But since the IMAC ligand substrate is itself a physical entity and a solid food stuff is a physical entity, it is wholly unclear as to how the skilled practitioner would contact a solid food sufficiently to remove nucleic acids. One can envision contacting the surface of the solid food, but to truly remove the nucleic acid contaminants would require passing the IMAC ligand substrate through the solid food stuff. This is physically impossible without completely disrupting the food. In

other words, the IMAC ligand substrate could not pass through solid food stuffs. With no guidance provided by the inventors in this regard, and no apparent prior art teaching of how this process might take place, an undue level of experimentation would be required of the skilled practitioner in order to carry out the invention as delineated by these claims.

As recited in original Claim 15, the foodstuff can be pretreated with a digestion enzyme, which will facilitate contact.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 10-13,21-25, and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Petty. The claims are drawn to methods of separating compounds using immobilized metal affinity chromatography. This is accomplished through the step of contacting a solution comprising compounds that contain shielded or non-shielded purine and/or pyrimidine moieties with a composition comprising IMAC ligands that are capable of binding non-shielded purine or pyrimidine moieties. This can occur through a column-type format. Additionally the method may [Page 11] also include the steps of separating the supernatant from the solid composition, or detecting compounds eluted from the column and identifying those compounds additionally eluting the bound compounds from the solid substrate. The non-shielded purine/pyrimidine moiety containing compounds may be various forms, of single-stranded nucleic acids and the shielded purine/pyrimidine moiety-containing compounds may be various forms of double stranded nucleic acids. Various limitations are placed on the relative purity of the non-shielded versus shielded purine/pyrimidine-containing compounds. The mixture of compounds may contain polyA mRNA and other mRNA species. The conditions may be controlled such that nucleic acids with different base compositions will elute at different times to allow to purify complementary sequences from each other.

25. Petty is drawn to protocols for the purification of 6-His-tagged proteins from celllysates using metal affinity chromatography, specifically using Ni2+ -NT A sepharose as the IMAC substrate. Pages 10.11.11-10.11.15 layout the basic protocol and pages 10.11.19-10.11.20 list the reagents used in the various protocols. Admittedly, Petty makes no mention of removal of single-stranded nucleic acids from the lysates to enrich for double-stranded nucleic acids in the

supernatant. However, this protocol uses bacterial celllysates, which necessarily will contain both double stranded DNA of any plasmids that may be contained as well as the genomic DNA and single stranded RNA. Evidence for Petty's acknowledgement of this can be found on page 10.11.13 where the lysates get treated with DNase I to reduce the viscosity of the lysates. The capability to bind to purine/pyrimidine-containing compounds is an inherent property of the Ne+-NTA resin used in this protocol. As such, the single stranded nucleic acids would tend to bind more tightly to the resin than the double stranded nucleic acid. The varying elution [Page 12] conditions would lead to differential release of different types of sequences and different sequence motifs would elute differentially as required by claims 29 and 30. Step 17 of the protocol, starting on page 10.11.14 establishes the step of analyzing the different factions for different properties as required in claims 13 and 28. Additionally the level of purity could easily be controlled through the stringency of binding conditions. Admittedly Petty does perform this protocol using E. coli, a prokaryotic organism, and consequently no polyA RNA would be present. Petty does however teach, on page 10.11.22, the use of eukaryotic expression systems, in which case polyA RNA would be present, fulfilling the limitations of claim 29. Thus the protocol of Petty anticipates claims 10-13,21-25, and 27-30 as written through the inherent properties [of] the Ne+ -NT A resin.

For clarity, the claims now recite that -- DNA and/or RNA— is present and is "collected".

Petty is from Current Protocols series. Petty's discussion is entirely focused on purifying *proteins*, not nucleic acids. Petty specifically focuses on purifying proteins bearing extra histidine amino acids encoded by pieces of DNA added to the gene for the protein of interest.

Petty's Figure 10.11B.1 shows DNA sequences, but they are not to be purified; they are used to add histidines to proteins to be purified. The section of Petty's page 10.11.11 marked "note" refers to another method of adding these histidine codons to the protein-encoding gene.

Petty's page 10.11.13 teaches operating only in the cold; this is not essential and is not preferred in many of the applications of the present invention.

Petty's Step 9 on page 10.11.13 adds a protein-destroying protease enzyme. The present invention avoids the need for this undesirable requirement of Petty. Petty's use of this DNA and RNA-destroying enzyme *teaches away* from the present invention, which collects the very moieties Petty seeks to destroy.

Petty's Step 11 on page 10.11.13 adds a DNA-destroying DNAse enzyme. In many of the applications of the present invention, this would be disastrous.

The Petty reference [page 10.11.XX?] teaches purifying only from E. coli. The present invention uses a much broader range of sources, including human clinical samples and enzymatically- synthesized mixtures.

In short, the Petty reference (like scores of other references) merely teaches the purifying of proteins, and a skilled person reading Petty would not learn anything of the present invention's valuable purifying of DNA and RNA.

> *26.Claims 16 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Hubert (1981). The claims are drawn to a method of purifying a compound that contains a purine or pyrimidine moiety comprising the steps of forming a mixture of the compound to be purified and contaminants, contacting the mixture with an !MAC ligand, separating the !MAC ligand compound-of-interest complex, and recovering the compound from the IMAC ligand.*
> *27.Hubert first makes a mixture of compounds: "Artificial mixtures to be tested were prepared from aqueous solutions (2.5 mg/ml) of different nucleotides"(page 164, second paragraph of Experimental). As seen in Figure 1, using a copper chelate affinity column, Hubert was then able to separate CMP !Tom GMP !Tom AMP. By recovering the fractions over time, the various bases are recovered through separation from the copper IMAC matrix of the column.*
> *Thus, Hubert purified individual compounds containing purine or pyrimidine moieties from a mixed solution as required by claims 16 and 32.*

Hurbert does not separate or collect DNA or RNA - he uses small mono and dinucleotides. Hurbert may not recover the products from the adsorbent. . Hurbert doesn't even test his procedure using a shielded purine or pyrimidine (Hurbert's small molecules do not form double-stranded structures in which the bases would be shielded). So Hurbert does not teach the presently claimed processes for separation of shielded from unshielded.

Also, Hubert does not teach how to purify even his small mono and dinucleotides from cells or tissues.

> *[Page 13]* ***Claim Rejections - 35 USC § 103***
> *28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:*
> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*
> *29. Claims 17 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hubert (1981) in view of Yarchoan (1986)(hereinafter Yarchoan-1), Yarchoan (1989)(hereinafter Yarchoan-2), or Alberts. Claims 17 and 33 further limit claims 16 and 32, respectively by limiting the compound of interest to be AZT, ddI, or coenzyme A (CoA). Hubert discloses all of the limitations of claims 16 and 32, as described above. Hubert does not disclose any mention of AZT, ddI, or CoA. Yarchoan-l discloses the structure of AZT (Figure 1), Yarchoan-2 discloses the structure of ddI (Figure 1), and Alberts discloses the structure of CoA (Figure 2-20). Both AZT and ddI are nucleotide analogs and CoA is a coenzyme containing adenine. One would have been motivated to use the purification method of Hubert for the purification of compounds of Yarchoan-l and -2 and Alberts because one would have had the full expectation of success since the purification of nucleotides is based on interactions of the metal ions with the nitrogenous bases of the nucleotides and all ofthe compounds contain either a purine or a pyrimidine moiety. "The dominant role played by the bases in the coordination mechanism, as suggested by our results, has already been demonstrated by crystallographic studies as well as experiments in solution"(Hubert, page 167, second paragraph). Additionally highly purified nucleotide-analog AIDS drugs and coenzymes are both preferred for their further use as drug or*

[Page 14] coenzyme. As all three of these compounds contain either a purine or a pyrimidine moiety, it would have been obvious to one of skill in the art to have used the purification method of Hubert to purify the compounds of Yarchoan-1 and -2 and Alberts.

Adding the two Yarchoan and the Albert references does not cure the above-discussed deficiencies of Hurbert.

Yarchoan, Weinhold et al. is a medical paper from The Lancet, which merely describes a clinical trial of the use of AZT for therapy of AIDS. It does not speak of, or even contemplate, metal-chelate affinity purification or any purification methods for any biomolecules, much less DNA and/or RNA, as now recited.

Yarchoan, Mitsuya et al. is a medical paper from Science, which describes a clinical trial of the use of ddI for therapy of AIDS. It does not speak of, or even contemplate, metal-chelate affinity purification or purification methods for any biomolecules, much less DNA and/or RNA, as now recited.. Serum uric acid was found to be *increased.* Thus, no purification occurs in Yarchoan at all. People eat the drug ddI, and their blood chemistry changes a bit.

Albert et al. is a classic textbook of cell biology, not bioseparations or biochemistry. The glycolytic pathway dscribed in this excerpt of Alberts is of interest primarily for the role of Acetyl CoA.

Coenzyme A (CoA; A for acyl) participates in activation of acyl groups in general, including the acetyl group derived from pyruvate. The coenzyme is derived metabolically from ATP, and the ATP-derived ring structure might be subject to metal-affinity adsorption. But Albert does not teach anything

about purifying it, by metal affinity or any other method. Albert just shows a picture of the molecule.

The JSTOR archive result is a search hit for Yarchoan, Mitsuya et al.,above.

> *Conclusion*
> *30.The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Bastian patent number 6,180,778 uses very similar technology to that claimed in the present invention. Any amendment to the claims should take this patent into account to avoid a new rejection based on overlapping scope.*

Bastian also does not use chelated metals to purify DNA and/or RNA, as is recited in the Claims, thus Bastian does not remedy the deficiencies of the other references as discussed above. Also Bastian [see Claim 1] requires two successive mineral supports, a cumbersome procedure.

> *Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick S. Riggins whose telephone number is (571) 272-6102.*
> *The examiner can normally be reached on M-F 7:00-3:30.*
> *If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781.*
> *The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.*
> *[Page 15] Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).*
> *Patrick Riggins, Ph.D. Examiner Art Unit 1636;*
> *James Ketter Primary Examiner*

Support from the specification for new Claims 34-37 is as follows:

34. [New] The method of claim 10 wherein the molecule containing a non-shielded purine or pyrimidine moiety is selected from among single-stranded DNA, (Table A) partially single-stranded DNA, (Table A) denatured DNA, (Paragraph 0021) fragmented DNA or RNA, (Paragraph 0189) plasmid DNA containing single-stranded regions, (Paragraph 0189) incomplete or imperfect PCR products, (Paragraph 0193) chain-terminated polymerase products, (Paragraph 0145) restriction endonuclease-digested DNA, (Paragraph 0225) single-stranded PNA, (Paragraph 0118) single-stranded primer, (Table A) single stranded RNA, (Table A) polyA mRNA (Table A) and/or messenger RNA, (Table A) and is removed from compounds that do not contain a non-shielded purine or pyrimidine moiety or group such as genomic DNA, (Table A) double-stranded plasmid DNA, (Table A) double-stranded PCR product, (Table A) double-stranded hybrid, (Table A) or double-stranded PNA (Paragraph 0118)

Claim 35 support: RNA supported in figures 5 and 8, paragraph 0058 and original claim 21;Single-stranded DNA supported by Figure 10 and paragraphs 0063 and 0138.
Claim 36 support: [0059]; [0062]; Fig 12; [0195]
Claim 37 support: [0059]; [0062]; Fig 12

No new matter has been added and no estoppel is involved. The changes were not required by prior art. No references were cited.

The two-month extension fee and any necessary (small entity) charges can be charged to USPTO Deposit Account 20336 of Technology Licensing Co. LLC.

To expedite prosecution, the Examiner is invited to suggest allowable subject matter. The Examiner is especially invited to telephone Applicants' Attorney if that would expedite prosecution and disposal of this Application.

Respectfully submitted,

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Enclosure: Replacement Figures 3, 5 & 8-11
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[Here insert Replacement Fig. 3, 5 & 8, and 9-11]

Amendments to the Drawings

Responding to Paragraph 6b of the Official Action (Spec. para 186 & 189)

(Corrected Figures 5 and 8 are enclosed herewith.)